In the specification:

Insert the paper copy of the Sequence Listing filed herewith following the Oath/Declaration.

Replace the paragraph beginning at page 8, line 4 with the following rewritten paragraph:

The interacting polypeptide/SIM preferably comprises the amino acid sequence PP(T/N)K or three out of four residues thereof. The three residues may be any three residues; ie the three residues need not be consecutive residues. Thus, the interacting polypeptide/SIM may comprise the amino acid sequence PPSK (SEQ ID NO:10) or PPQK (SEQ ID NO:3) ie a residue with an aliphatic hydroxyl side chain or an amide side chain may be present between the PP and K residues. It is strongly preferred that an alanine residue is not present instead of the T/N residue, ie between the PP and K residues.

Replace the paragraph beginning at page 9, line 18 with the following rewritten paragraph:

Thus, the SIM (and polypeptide) may comprise at least 8, 9 or 10 (preferably 10 or 11) of the specified residues (ie not residues designated by an X) of the amino acid sequence D/E-Hyd-$(X)_n$-P-P-(N/T)-K-(T/S)-(I/V)-$(X)_m$-(D/E)-(M/V/I)-$(X)_k$-P (SEQ ID NO:24)

wherein m= 0 to 7; k= 0 to 8 or 12; n = 0 to 15 or 18.

Replace the paragraph beginning at page 10, line 1 with the following rewritten paragraph:

A polypeptide of less than 32 amino acids in length may comprise a SIM and be capable of interacting with a Smad polypeptide without comprising all elements of the D/E-Hyd-$(X)_n$-P-P-(N/T)-K-(T/S)-(I/V)-$(X)_m$-(D/E)-(M/V/I)-$(X)_k$-P (SEQ ID NO:24) motif; for example the polypeptide may be a polypeptide as defined below and in claim 12 which does not have residues corresponding to the D/E-Hyd-$(X)_n$ residues, because the N-terminal amino acids of the polypeptide correspond to the PPNK motif (SEQ ID NO:1) (for example a polypeptide consisting of the amino acid sequence PPNKTITPDMNVRIPPI) (SEQ ID NO:4).

Replace the paragraph beginning at page 10, line 19 with the following rewritten paragraph:

By "interacting with" is included the meaning of "binding to", for example detectably binding to, for example binding detectable using any method of detecting protein/protein binding as indicated below, for example co-immunoprecipitation or a surface plasmon resonance technique. The term "polypeptide" in connection with the interacting polypeptide includes peptides as small as the peptide PPNK (SEQ ID NO:1)or PPTK (SEQ ID NO:2). The invention includes a polypeptide of less than 32, 31 or 30 amino acids in length comprising the amino acid sequence PP(T/N)K.

Replace the paragraph beginning at page 21, line 17 with the following rewritten paragraph:

It is preferred that the Smad polypeptide, for example Smad2 or Smad3 polypeptide is a polypeptide which consists of the amino acid sequence of the Smad2 or Smad3 polypeptide as shown in Macias-Silva *et al* (1996) *Cell* **87**, 1215-1224 (human Smad2); Graff *et al* (1996) *Cell* **85**, 479-487 (*Xenopus* Smad2); Zhang *et al* (1996) *Nature* **383**, 168-172 (human Smad3) or Figure 12 (*Xenopus* Smad3), or naturally occurring allelic variants thereof and fusions thereof. A preferred fusion may be a GST fusion, for example as described in Example 1 or any other fusion described in Example 1 or a Myc fusion as described, for example, in Chen *et al* (1997). A further preferred fusion may have the tag Glu-Phe-Met-Pro-Met-Glu (SEQ ID NO:60) (termed EE-tag) or a His, HA or FLAG tag, as well known to those skilled in the art.

Replace the paragraph beginning at page 24, line 13 with the following rewritten paragraph:

As indicated above, it is preferred that the interacting polypeptide further has an acidic (ie negatively charged) amino acid residue present at a position from 3 to 10, preferably 4 to 5 residues C-terminal of the amino acid sequence corresponding to the PP(T/N)K motif (and may be immediately followed by a hydrophobic residue, for example M, V or I), and/or a proline residue present at a position from 5 to 20 residues C-terminal of the amino acid sequence corresponding to the PP(T/N)K motif, as discussed above. The acidic (negatively charged)

71. (Previously Amended) A method of identifying a polypeptide that is capable of interacting with a Smad polypeptide, comprising examining the sequence of a polypeptide and determining that the polypeptide comprises a Smad Interaction Motif (SIM), for example the amino acid sequence PP(T/N)K or three out of four residues thereof.

72. (Currently Amended) The method of claim 71 comprising determining that the polypeptide comprises at least 8, 9 or 10 of the specified residues other than X of the amino acid sequence D/E-Hyd-$(X)_n$-P-P-(N/T)-K-(T/S)-(I/V)-$(X)_m$-(D/E)-(M/V/I)-$(X)_k$-P (SEQ ID NO:24)

wherein m= 0 to 7; k= 0 to 8 or 12; n = 0 to 15 or 18.

73. (Previously Amended) The method of claims 71 or 72 comprising determining that the polypeptide comprises the amino acid sequence PP(T/N)K.

74. (Previously Amended) The method of claims 71 or 72 further comprising determining that an acid amino acid residue is present at a position from 3 to 10 residues C-terminal of the amino acid sequence PP(T/N)K or amino acid sequence corresponding to the PP(T/N)K motif, and/or a proline residue is present at a position from 5 to 20 residues C-terminal of the amino acid sequence PP(T/N)K or amino acid sequence corresponding to the PP(T/N)K motif.

75. (Previously Amended) A method of identifying a compound capable of disrupting or preventing the interaction between a Smad polypeptide and a target polypeptide that is (1) a transcription factor capable of interacting with the said Smad polypeptide and/or (2) a polypeptide capable of interacting with the said Smad polypeptide, the interaction requiring a-helix2 of the said Smad polypeptide or (3) a polypeptide comprising the amino acid sequence PP(T/N)K, the method comprising measuring the ability of the compound to disrupt or prevent the interaction between the Smad polypeptide and a polypeptide or molecule according to any one of claims 50-55 and 63.

76. (Previously Amended) A compound identified by or identifiable by the method of claim 73 or claim 74.

77. (Previously Amended) A kit comprising a Smad polypeptide and a polypeptide or molecule according to any one of claims 50-55, 63 and 66.

78. (Previously Amended) A method of disrupting or preventing the interaction between a Smad polypeptide and a target polypeptide that is (1) a transcription factor capable of interacting with the said Smad polypeptide and/or (2) a polypeptide capable of interacting with the said Smad polypeptide, the interaction requiring a-helix2 of the said Smad polypeptide, the method comprising exposing the Smad polypeptide to a polypeptide or molecule according to any one of claims 50-55 and 63.

79. (Previously Amended) A method of disrupting or preventing the interaction between a Smad polypeptide and a polypeptide comprising the amino acid sequence PP(T/N)K wherein the Smad polypeptide is exposed to a polypeptide or molecule according to any one of claims 50-55 and 63.

80. (Previously Amended) The method of claim 78 wherein the Smad polypeptide is Smad2 or Smad3.

81. (Previously Amended) A composition comprising the polypeptide according to any one of claims 50-55 and a pharmaceutically acceptable carrier.

82. (Previously Amended) A method of modulating activin or TGFb signalling in a cell in vitro comprising exposing the cell to the polypetpide of any one of claims 50-55.

83. (Previously Amended) A method of modulating activin or TGFb signalling in a cell in vivo comprising exposing the cell to the polypeptide of any one of claims 50-53.

84. (Previously Amended) The method of claim 83 wherein the cell is a late stage tumor cell.

85. (Previously Amended) A method for modulating activin or TGFb signaling in a patient comprising administering the polyeptide of any of claims 50-55.

86. (Previously Amended) A method for treating cancer comprising administering the polypeptide of any one of claims 50-55.

87. (Previously Amended) A method for treating a patient in need of reducing extracellular matrix deposition, encouraging tissue repair and/or regeneration, tissue remodelling or healing of a wound, injury or surgery, or reducing scar tissue formation arising from injury to the brain comprising administering the polypeptide of any of claims 50-55.

88. (Previously Amended) A method for treating a patient with or at risk of end-stage organ failure, pathologic extracellular matrix accumulation, a fibrotic condition, disease states associated with immunosuppression (such as different forms of malignancy, chronic degenerative diseases, and AIDS), diabetic nephropathy, tumour growth, kidney damage (for example obstructive neuropathy, IgA nephropathy or non-inflammatory renal disease) or renal fibrosis comprising administering the polypeptide of any of claims 50-55.

89. (Previously Amended) A substantially pure complex comprising: (1) a Smad2 or Smad3 polypeptide, (2) a Smad4 polypeptide and (3) a Mixer and/or Milk and/or Bix2/3 and/or FAST3 polypeptide.

90. (Previously Amended) A preparation comprising: (1) Smad2 or Smad3 polypeptide, (2) a Smad4 polypeptide and (3) a Mixer and/or Milk and/or Bix2/3 and/or FAST3 polypeptide (in the form of a complex or otherwise) when combined with other components ex vivo, said other components not being all of the components found in the cell in which said (1)

Smad2 or Smad3 polypeptide, (2) a Smad4 polypeptide and (3) a Mixer and/or Milk and/or Bix2/3 and/or FAST3 polypeptide (in the form of a complex or otherwise) are naturally found.

91. (Previously Amended) A cell comprising: 1) a recombinant polynucleotide suitable for expressing a transcription factor that is capable of interacting with a Smad polypeptide and 2) a recombinant polynucleotide comprising a reporter gene driven by a promoter with a binding site for the said transcription factor.

92. (Previously Amended) A stable cell line cell comprising a reporter gene driven by a promoter with one or more binding sites for an activated Smad, wherein the Smad is activated in the cell by exposure of the cell to TGFb.

93. (Previously Amended) The cell according to claims 91 or 92 wherein the reporter gene expresses luciferase, secreted alkaline phosphatase (SEAP), CAT or a green fluorescent protein (GFP).

94. (Previously Amended) A method of identifying a compound capable of modulating TGFb-dependent transcription wherein the effect of the compound on expression of the reporter gene in a cell according to claims 91 or 92 is measured, following treatment of the cell with TGFb.

95. (Previously Amended) A method of identifying a compound capable of modulating TGFb-dependent transcription wherein the effect of the compound on TGFb-signalling-dependent invasive behaviour of a stably-transformed cell line cell, for example in collagen gels, is measured and a compound that reduces invasive behaviour is selected.

96. (Previously Amended) The method of claim 95 wherein the stably-transformed cell line is a MDCK cell line that is capable of expressing recombinant active Raf-1.